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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/920,805	08/03/2001	Sciichi Shibamura	P21313	7834

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EXAMINER
HOLLERAN, ANNE L

ART UNIT	PAPER NUMBER
1642	6

DATE MAILED: 07/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Applicati n No.	Applicant(s)	
	09/920,805	SHIBAMURA ET AL.	
	Examiner	Art Unit	
	Anne Holleran	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,8-15 and 24* is/are rejected.

7)☒ Claim(s) *2-7,10 and 16-23* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 October 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. *09147,839* .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *2,3* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. The preliminary amendment filed October 7, 2002 (Paper No. 5) is acknowledged. Claims 1, and 13-15 were amended.

2. Claims 1-24 are pending and examined on the merits.

3. The corrected or substitute drawings were received on October 7. The amendments to the drawings are approved.

4. Claim 10 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 10, dependent from claim 1, does not appear to change the scope of claim 1, because the list of substances is the same as that in claim 1.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Claim 13 is rejected under 35 U.S.C. 102(b) as being anticipate by either Mishra (Acta Chimica Hungarica 116(1): 5-12, 1984) or Kapoor (J. of Luminescence, 22: 429-439, 1981).

Claim 13 is drawn to an agent that comprises a substance that is a glycerophospholipid, fatty acid or surfactant that is a saccharide derivative having fluorescence intensity enhancing effect.

Either Mishra or Kapoor teaches that surfactants increase fluorescence intensity of fluorescent dyes. Mishra teaches that surfactants increase the fluorescence intensity of eosin, and Kapoor teaches that surfactants increase the fluorescence intensity of rose-bengal dye. Both Mishra and Kapoor teach an example of a surfactant that is a saccharide derivative (see page 430 in Kapoor, Tween; see pages 6 and 8, effect of Tweens). Thus, Mishra or Kapoor teach agents that are the same as that claimed.

6. Claim 13 is rejected under 35 U.S.C. 102(e) as being anticipated by Klemt (U.S. Patent 5,677,192; Oct. 14, 1997; effective filing date Mar. 18, 1996; cited in IDS).

Klemt teaches the compound octylglucoside, which is a saccharide derivative having fluorescence intensity enhancing effect. Thus, Klemt teaches agents that are the same as that claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1, and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Karandikar (U.S. Patent 6,207,464; issued Mar. 27, 2001; effective filing date June 7, 1995) in

view of either Mishra (Acta Chimica Hungarica 116(1): 5-12, 1984) or Kapoor (J. of Luminescence, 22: 429-439, 1981).

Claims 1, and 10 are drawn to compositions comprising an antibody bound with a fluorescent functional group comprising an indocyanine green derivative which is capable of being excited to cause fluorescence, and at least one substance that enhances fluorescence intensity of the fluorescent functional group, where the substance is either a glycerophospholipid, a fatty acid or a surfactant, wherein the surfactant is a saccharide derivative having fluorescence intensity enhancing effect. The scope of the term fluorescent functional group comprising an indocyanine green derivative which is capable of being excited to cause fluorescence" is interpreted broadly as drawn to almost any fluorescent functional group, because the structural limitation is that of an "indocyanine green derivative", which may encompass any part of an indocyanine green molecule. Claim 10 appears to be of the same scope as that of claim 1.

Karandikar teaches fluorescent functional groups bound to antibodies (see col. 6, lines 60-65; col. 11, lines 51-58).

Karandikar fails to teach a composition comprising a fluorescent functional group bound to an antibody in combination with a substance that is a glycerophospholipied, fatty acid or surfactant that is a saccharide derivative having fluorescence intensity enhancing effect.

However, either Mishra or Kapoor teaches that surfactants increase fluorescence intensity of fluorescent dyes. Mishra teaches that surfactants increase the fluorescence intensity of eosin, and Kapoor teaches that surfactants increase the fluorescence intensity of rose-bengal dye. Both Mishra and Kapoor teach an example of a surfactant that is a saccharide derivative (see page 430 in Kapoor, Tween; see pages 6 and 8, effect of Tweens). Thus, it would have been prima facie

obvious to one of ordinary skill in the art at the time the invention was made to have made a composition as claimed by using the fluorescently labeled antibody of Karandikar and combining it with the surfactants taught by either Kapoor or Mishra. One would have been motivated to have added the surfactants of Kapoor or Mishra to the labeled antibody of Karandikar, because Kapoor or Mishra teach that the addition of surfactants increases fluorescence intensity, which is a desirable effect because an increase in fluorescence intensity will increase the signal to noise ratio of an assay.

8. Claims 1, 10, 12, 14, 15 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Karandikar (U.S. Patent 6,207,464; issued Mar. 27, 2001; effective filing date June 7, 1995) in view of either Mishra (Acta Chimica Hungarica 116(1): 5-12, 1984) or Kapoor (J. of Luminescence, 22: 429-439, 1981) and further in view of Sykes et al (U.S. 6,313,274; issued Nov. 6, 2001; effective filing date May 25, 1995).

Claims 1, 10 and 12 are drawn to compositions comprising an antibody bound with a fluorescent functional group comprising an indocyanine green derivative which is capable of being excited to cause fluorescence, and at least one substance that enhances fluorescence intensity of the fluorescent functional group, where the substance is either a glycerophospholipid, a fatty acid or a surfactant, wherein the surfactant is a saccharide derivative having fluorescence intensity enhancing effect. The scope of the term fluorescent functional group comprising an indocyanine green derivative which is capable of being excited to cause fluorescence" is interpreted broadly as drawn to almost any fluorescent functional group, because the structural limitation is that of an "indocyanine green derivative", which may encompass any part of an

indocyanine green molecule. The antibody is an anticancer antibody. Claims 14, 15 and 24 are drawn to methods for immunohistochemical diagnosis, comprising contacting either a tumor cell or a malignant neoplasia with the composition as recited above for claim 1, allowing the composition to bind to the tumor cell of malignant neoplasia, thereby staining the cell or the malignant neoplasia. The neoplasia of epithelial tissues is esophagus cancer, stomach cancer or large bowel cancer.

Karandikar fails to teach compositions comprising antibodies that bind to tumor antigens. The combination of Karandikar with either of Mishra or Kapoor fails to teach compositions comprising antibodies that bind to tumor antigens. However, Sykes teaches antibodies that may be labeled with a fluorophore that bind to tumor antigens such as tumor antigens of colon cancer (see col. 15, lines 17-21; col. 8, lines 3-23). Karandikar's fluorescent label may be conjugated to an antibody via sulphydryl groups (see col. 10, lines 4-11). Thus, it would have been prima facie obvious to one of ordinary skill in the art a the time the invention was made to have used the antibodies of Sykes as the target compound for the fluorescent compounds of Karandikar, and further to have added surfactants as taught by Mishra or Kapoor for the enhancement of fluorescence to make the claimed compositions and methods.

9. Claims 1, and 8-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Karandikar (U.S. Patent 6,207,464; issued Mar. 27, 2001; effective filing date June 7, 1995) in view of Klemt (U.S. Patent 5,677,192; Oct. 14, 1997; effective filing date Mar. 18, 1996; cited in IDS).

Claims 1, and 10 are drawn to compositions comprising an antibody bound with a fluorescent functional group comprising an indocyanine green derivative which is capable of being excited to cause fluorescence, and at least one substance that enhances fluorescence intensity of the fluorescent functional group, where the substance is either a glycerophospholipid, a fatty acid or a surfactant, wherein the surfactant is a saccharide derivative having fluorescence intensity enhancing effect. The scope of the term fluorescent functional group comprising an indocyanine green derivative which is capable of being excited to cause fluorescence" is interpreted broadly as drawn to almost any fluorescent functional group, because the structural limitation is that of an "indocyanine green derivative", which may encompass any part of an indocyanine green molecule. Claim 10 appears to be of the same scope as that of claim 1.

Karandikar teaches fluorescent functional groups bound to antibodies (see col. 6, lines 60-65; col. 11, lines 51-58).

Karandikar fails to teach a composition comprising a fluorescent functional group bound to an antibody in combination with a substance that is a glycerophospholipied, fatty acid or surfactant that is a saccharide derivative having fluorescence intensity enhancing effect.

However, Klemt teaches that compounds such as octylglucoside increase luminescence intensity. Thus, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have made a composition as claimed by using the fluorescently labeled antibody of Karandikar and combining it with octylglucoside as taught by Klemt. One would have been motivated to have added octylglucoside as taught by Klemt to the labeled antibody of Karandikar, because an increase in fluorescence intensity leads to an increase in sensititivity of assays employing a fluorescently labeled antibody.

10. Claims 1, 10-12, 14, 15 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ito (Bioorganic and Medicinal Chemistry Letters5(22): 2689-2694, 1995; cited in IDS) in view of Mishra (Acta Chimica Hungarica 116(1): 5-12, 1984) or Kapoor (J. of Luminescence, 22: 429-439, 1981) and further in view of Sykes et al (U.S. 6,313,274; issued Nov. 6, 2001; effective filing date May 25, 1995).

Claims 1, 10 and 12 are drawn to compositions comprising an antibody bound with a fluorescent functional group comprising an indocyanine green derivative which is capable of being excited to cause fluorescence, and at least one substance that enhances fluorescence intensity of the fluorescent functional group, where the substance is either a glycerophospholipid, a fatty acid or a surfactant, wherein the surfactant is a saccharide derivative having fluorescence intensity enhancing effect. The antibody is an anticancer antibody. Claims 14, 15 and 24 are drawn to methods for immunohistochemical diagnosis, comprising contacting either a tumor cell or a malignant neoplasia with the composition as recited above for claim 1, allowing the composition to bind to the tumor cell of malignant neoplasia, thereby staining the cell or the malignant neoplasia. The neoplasia of epithelial tissues is esophagus cancer, stomach cancer or large bowel cancer.

Ito teaches antibodies labeled with succinamide esters of indocyanine green. Ito fails to teach an antibody that binds to a cancer antigen, and fails to teach compositions comprising at least one substance that enhances fluorescence intensity of the fluorescent functional group, where the substance is either a glycerophospholipid, a fatty acid or a surfactant, wherein the surfactant is a saccharide derivative having fluorescence intensity enhancing effect.

However, Sykes teaches antibodies that may be labeled with a fluorophore that bind to tumor antigens such as tumor antigens of colon cancer (see col. 15, lines 17-21; col. 8, lines 3-23), and either Mishra or Kapoor teach fluorescence enhancing substances. Thus, it would have been prima facie obvious to one of ordinary skill in the art a the time the invention was made to have used the antibodies of Sykes as the antibody that is bound to the succinamide esters of indocyanine green of Ito, and further to have added surfactants as taught by Mishra or Kapoor for the enhancement of fluorescence to make the claimed compositions and methods.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the Office should be directed to Anne Holleran, Ph.D. whose telephone number is (703) 308-8892. Examiner Holleran can normally be reached Monday through Friday, 9:30 am to 2:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, Ph.D. can be reached at (703) 308-3995.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist at telephone number (703) 308-0196.

Anne L. Holleran
Patent Examiner
June 29, 2003

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